

## REMARKS

### *Status of the Claims*

Claims 1-20, 36, and 37 are pending. Claims 2, 3, 6, 9-11, and 14-16 are amended. Claim 37 is newly added. Support for the amendments and new claim may be found throughout the application as originally filed.<sup>1</sup> No new matter is added.

### *Withdrawn Rejections*

Applicant greatly appreciates the Examiner's withdrawal of all previous rejections.

### *Interview Summary*

On April 27, 2010, Applicant, Applicant's undersigned representative, and Examiner Perreira conducted a telephonic interview.

During the interview, Applicant and Applicant's representative explained that one of skill in the art would not have combined Brow et al. (J. Non-Crystalline Solids 1990, 120: 172-177, hereinafter "Brow") and/or Yashchishin et al. (Glass and Ceramics 1997, 54: 6-8; hereinafter "Yashchishin") with Glajch (U.S. Patent No. 6,455,024; hereinafter "Glajch"). Applicant and Applicant's representative pointed out, *inter alia*, that the claims relate to bioabsorbable and biocompatible materials used for therapy, whereas Brow and Yashchishin relate to bulk glass materials, which are not bioabsorbable or biocompatible, and are used for industrial purposes.

Applicant and Applicant's representative greatly appreciate and thank Examiner Perreira for her time and consideration during the interview.

### *Rejections Under 35 U.S.C. § 103*

Claims 1-5, 8, 10-16, 18-20, and 36 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Glajch in view of Brow and Yashchishin, and in further view of Day et al. (U.S. Patent No. 5,011,797, hereinafter "Day").

The USPTO contends that Glajch discloses a glass particle/implant that comprises radionuclides and has nitrogen incorporated in the glass, but does not disclose a nitrogen layer on the surface of the particle/implant.<sup>2</sup> To remedy this missing teaching, the USPTO cites Brow and Yashchishin, and asserts that it would have been obvious to dope Glajch's phosphate glass using

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<sup>1</sup> See, e.g., Specification, ¶¶ [018], [019], and [065].

<sup>2</sup> See Office Action, pages 3 and 5.

Brow's and/or Yashchishin's method to generate a nitrogen layer on the surface of the phosphate glass "to improve its chemical stability."<sup>3</sup>

Applicant respectfully traverses.<sup>4</sup>

**A. There is no reason to combine Brow and/or Yashchishin with Glajch.**

**1. There is no reason to add a nitrogen-rich surface layer to Glajch's already nitrated composition.**

In its last response, Applicant explained that Glajch incorporates nitrogen into glass by melting phosphate in ammonia at high temperatures.<sup>5</sup> As a result, nitrogen is distributed uniformly throughout Glajch's glass when formed from the melted liquid. Glajch states that nitrating the starting glass "is expected to decrease the dissolution rate of the solid in water and increase the chemical stability of the solid."<sup>6</sup> Accordingly, Glajch's composition already contains enough nitrogen to improve the chemical stability of the composition.

Applicant submits that there is no reason to add a nitrogen surface layer to Glajch's already nitrated composition. Indeed, neither the cited references nor the USPTO provides any reason why one of skill in the art would modify Glajch's already nitrated composition by adding more nitrogen—in the form of a nitrogen-rich surface layer, the surface layer being of greater durability than the base glass matrix. Moreover, if a phosphate glass is already nitrated through melting in ammonia (i.e., Glajch's method), there is no reason to have additional surface nitrating since melting is generally done at a much higher temperature than surface nitrating and thus is likely to achieve a much higher nitrogen content as compared to surface nitrating (see discussion below). As such, there is no obvious benefit to include an additional nitrating step. Accordingly, there is no reason to combine Brow's and/or Yashchishin's teachings with Glajch's teachings.

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<sup>3</sup> See *id.* at page 6.

<sup>4</sup> As discussed herein, the combination of Glajch, Brow, and Yashchishin does not teach or suggest the claimed implant materials (e.g., the combination does not teach or suggest a nitrogen-rich surface layer). The USPTO cites Day for teaching treatment of radiation synovectomy and arthritis. See Office Action, page 6. Accordingly, because (i) Day does not teach a nitrogen-rich surface layer, and (ii) the USPTO does not rely on Day as teaching a nitrogen-rich surface layer, Applicant submits that Day does not remedy the deficiencies of Glajch, Brow, and Yashchishin.

<sup>5</sup> See Applicant's response, filed April 5, 2010, pages 5 and 6.

<sup>6</sup> Glajch, col. 5, lines 45-47.

**2. Brow's and Yashchishin's nitriding methods would likely crystallize and/or sinter Glajch's glass powders—precisely what the claimed implant materials avoid.**

The claimed invention involves forming a nitrogen-rich surface layer. The specification teaches that this nitriding step occurs near or above softening temperatures of the particular glass.<sup>7</sup> This temperature is “chosen such that undesirable outcomes such as sintering or recrystallization of the particulates are avoided.”<sup>8</sup> Accordingly, in order to arrive at the claimed implant materials, one of skill in the art would avoid nitriding methods that would result in these undesirable outcomes.

**a. Brow's methods would crystallize Glajch's glass.**

Glajch's base glass has a peak crystallization temperature ( $T_c$ ) of 360°C<sup>9</sup> and crystallization range from 320°C to 400°C.<sup>10</sup> Brow suggests nitriding glass near the glass transition temperature ( $T_g$  = 345°C),<sup>11</sup> which is close to the peak crystallization temperature (360°C) and within the crystallization range (320°C to 400°C). Therefore, if one of skill in the art applied Brow's methods to Glajch, which they would not, this hypothetical method would likely prepare a crystallized glass—glass that the instant invention sought to avoid. As such, one of skill in the art would be discouraged from combining Brow with Glajch to attempt to arrive at the claimed implant materials.

**b. Brow's and Yashchishin's methods would sinter Glajch's glass.**

Glajch's base glass has a softening temperature ( $T_s$ ) of 262°C.<sup>12</sup> Brow and Yashchishin perform surface nitriding near glass transition temperature ( $T_g$ ) and below  $T_g$ , respectively.<sup>13</sup> Specifically, Brow suggests nitriding phosphate glasses at 345°C,<sup>14</sup> and Yashchishin nitrides phosphate glasses at 400-500°C.<sup>15</sup> As such, if one of skill in the art applied Brow's or Yashchishin's methods to Glajch, which they would not, these hypothetical methods would likely fuse or sinter

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<sup>7</sup> See, e.g., Specification, ¶ [095].

<sup>8</sup> *Id.*

<sup>9</sup> See Reidmeyer, page 190, Table 2. As discussed herein, Glajch's nitriding method (i.e., the glass formed) is based on Reidmeyer's method.

<sup>10</sup> See *id.* at page 191, Figure 4.

<sup>11</sup> See Brow, Page 172, abstract.

<sup>12</sup> See Reidmeyer, page 190, Table 2.

<sup>13</sup> See Brow, Page 172, abstract; see also Yashchishin, page 6, abstract.

<sup>14</sup> See Brow, Page 172, abstract.

<sup>15</sup> See Yashchisin, page 8, left column, middle of first full paragraph.

Glajch's powder into a solid block—glass that the instant invention sought to avoid—because Brow's and Yashchishin's nitriding temperatures are much higher than that softening temperature of Glajch's base glass. As such, one of skill in the art would be discouraged from combining Brow or Yashchishin with Glajch to attempt to arrive at the claimed implant materials.

**3. There is no reason to substitute Glajch's nitriding method with a nitriding method that produces a less stable glass that has a faster dissolution rate.**

**a. Brow's and Yashchishin's methods would produce glass that is less stable than glass produced using Glajch's method.**

Glajch teaches that nitriding phosphate starting glass “produces glasses containing up to 12 wt % nitrogen.”<sup>16</sup> As discussed above, Glajch teaches that this process “increases the chemical stability” of the glass. Brow's and Yashchishin's surface nitriding methods produce glasses that incorporate “up to 3-5%”<sup>17</sup> and “0.5-2%”<sup>18</sup> nitrogen, respectively, i.e., amounts far lower than that of Glajch. Assuming that one of skill in the art would have substituted Brow's and/or Yashchishin's nitriding methods for Glajch's nitriding method, which they would not, they would have obtained a less stable glass. Accordingly, Applicant submits that one of skill in the art would have no reason to substitute Brow's and/or Yashchishin's inferior nitriding methods for Glajch's nitriding method.<sup>19</sup>

**b. Brow's and Yashchishin's methods would produce a glass that dissolves significantly faster than glass produced using Glajch's method.**

As discussed above, Glajch teaches that its nitriding process “is expected to decrease the dissolution rate of the solid in water.” Glajch's nitriding method is based on a method disclosed by Reidmeyer et al. (J. Non-Crystalline Solids 1986, 85: 186-203, hereinafter “Reidmeyer”).<sup>20</sup> Reidmeyer teaches that the dissolution rate of glass treated with 11.75 % nitrogen (i.e., Reidmeyer/Glajch nitriding method) is 1000 times slower than the dissolution rate of base glass (i.e., glass not treated

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<sup>16</sup> See Glajch, col. 5, lines 45-50; see also Office Action, page 3 (“the phosphate glass may incorporate up to 12 wt % nitrogen”).

<sup>17</sup> See Brow, abstract (“...analyses show that nitrogen is chemically incorporated into the glass structure at levels up to 3-5%.”).

<sup>18</sup> See Yashchishin, page 8.

<sup>19</sup> See M.P.E.P § 2143.01 (“If [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.”) (citing *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)).

<sup>20</sup> See Glajch, col. 5, lines 40-44.

with nitrogen).<sup>21</sup> Yashchishin and Brow suggest that the dissolution rate of their treated glass is only about 3 to 6 times<sup>22</sup> and 10 times,<sup>23</sup> respectively, slower than the dissolution rate of base glass. As such, one of skill in the art would understand that glass treated using Yashchishin's or Brow's method would dissolve significantly faster than glass made using Glajch's method. Accordingly, there is no reason why one of skill in the art would substitute Glajch's nitriding method, which seeks to decrease the dissolution rate, with a nitriding method that results in a faster dissolution rate than that of Glajch.<sup>24</sup>

In view of the foregoing, Applicant submits that there is no reason to combine Brow and/or Yashchishin with Glajch. Accordingly, Applicant respectfully requests withdrawal of this rejection.

**B. Combining Brow's and/or Yashchishin's nitriding methods with Glajch would not produce the claimed implant materials.**

The claimed implant materials comprise a nitrogen-rich surface layer that assists in, for example, preventing the premature start of bioresorption and the premature release of radioisotopes. Delaying bioresorption and leakage of radioisotopes is advantageous for various radiotherapies such as the treatment of liver cancer. As such, one of skill in the art would understand that, in order for the claimed implant materials to work for their intended purpose, the nitrogen-rich surface layer would necessarily surround the implant materials.

Glajch teaches a method of making phosphate glass particles by melting phosphate glass into a "bulk" glass and crushing the phosphate glass into particles.<sup>25</sup> Brow and Yashchishin disclose methods of nitriding "bulk" materials.<sup>26</sup>

Assuming one of skill in the art had a reason to apply Brow's and/or Yashchishin's methods to Glajch, which they would not, the skilled artisan would nitride Glajch's bulk glass and then crush the nitrified bulk glass into particles. One of skill in the art would understand that crushing bulk

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<sup>21</sup> See Reidmeyer, page 187, Table 1 (showing the dissolution rate of base glass as  $1.1 \times 10^{-3}$  compared to glass treated with 11.75 % nitrogen as  $1.9 \times 10^{-6}$ ).

<sup>22</sup> See Yashchishin, page 8 (teaching that its method improves the chemical stability of phosphate glasses by 3 to 6 times).

<sup>23</sup> See Brow, abstract ("For example, the dissolution rate a sodium-barium phosphate glass ( $T_g = 345^\circ\text{C}$ ) decreased by over an order of magnitude"). One of skill in the art would understand that an order of magnitude means 10 times.

<sup>24</sup> See Footnote 19, *supra*.

<sup>25</sup> See Glajch, col. 12, lines 7-17, Example 2.

<sup>26</sup> See Brow, page 172, under "Introduction" (disclosing glasses designed for sealing to high expansion metals); *see also* Yashchishin, page 8, last paragraph (disclosing optical glasses for lenses).

glass into particles will necessarily result in particles that do not have any nitrogen, let alone a nitrogen-rich surface layer (e.g., a particle formed from the middle of the bulk glass would not have any nitrogen on its surface). Indeed, these particles would not result in the claimed implant materials, nor would they be useful for radiotherapy.<sup>27</sup> Accordingly, even assuming one of skill in the art substituted Brow's and/or Yashchishin's nitriding methods for Glajch's nitriding method, this hypothetical method would not produce the claimed implant materials.<sup>28</sup>

Applicant also submits that one of skill in the art would not have a reason to apply Brow's and/or Yashchishin's methods to Glajch's crushed glass. First, Brow and Yashchishin do not teach or suggest nitriding microdimensional particles such as crushed glass. Rather, these references relate to nitriding "bulk" glasses. Second, as discussed above, there is no reason add a nitrogen-rich layer to Glajch's already nitrified particle. Third, as discussed above, Brow's and Yashchishin's methods would likely crystallize and/or sinter Glajch's glass particles. Fourth, as discussed above, there is no reason to substitute Glajch's nitriding method with Brow's or Yashchishin's methods, which would produce a less stable glass that dissolves significantly faster than glass produced using Glajch's glass.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

Claims 1-5, 8-11, 13-16, 18-20, and 36 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Glajch in view of Brow and Yashchisin, and in further view of Gilchrist et al. (U.S. Patent No. 6,143,318, hereinafter "Gilchrist").

As discussed above, the combination of Glajch, Brow, and Yashchishin does not teach or suggest resorbable implant materials comprising, *inter alia*, a nitrogen-rich surface layer formed on the resorbable base glass matrix, the surface layer being of greater durability than the base glass matrix. Gilchrist does not remedy the deficiencies of Glajch, Brow, and Yashchishin. Indeed, Gilchrist is silent regarding the use of nitrogen, let alone forming a nitrogen-rich layer on the surface of a resorbable base glass matrix. Accordingly, because the combination of Glajch, Brow, Yashchishin, and Gilchrist does not teach or suggest each and every element of claim 1 or 36, this combination does not render obvious any of the claims.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

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<sup>27</sup> These particles would also render Glajch unsuitable for its intended purpose. See Footnote 19, *supra*.

<sup>28</sup> The same is true if one of skill in the art combined the nitriding methods of Glajch, Brow, and Yashchishin. Indeed, this combination would still produce materials not having a nitrogen-rich surface layer.

Claims 1-8, 10-20, and 36 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Glajch in view of Brow and Yashchisin, and in further view of Wong et al. (U.S. Pub. No. 2004/0131543, hereinafter “Wong”).

As discussed above, Glajch, Brow, and Yashchishin does not teach or suggest resorbable implant materials comprising, *inter alia*, a nitrogen-rich surface layer formed on the resorbable base glass matrix, the surface layer being of greater durability than the base glass matrix. Wong does not remedy the deficiencies of Glajch, Brow, and Yashchishin. Indeed, Wong is silent regarding the use of nitrogen, let alone forming a nitrogen-rich layer on the surface of a resorbable base glass matrix. Accordingly, because the combination of Glajch, Brow, Yashchishin, and Wong does not teach or suggest each and every element of claim 1 or 36, this combination does not render obvious any of the claims.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

**CONCLUSION**

In view of the above remarks, early notification of a favorable consideration is respectfully requested. An indication of allowance of all claims is respectfully requested.

This response is being filed within the three-month time period set forth in the Office Action. Accordingly, no fees are due. Should any fees be due to enter and consider this response, however, the USPTO is authorized to charge these fees to **Deposit Account No. 50-0206**.

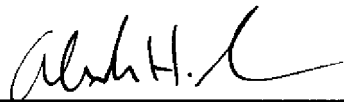
If the Examiner has any questions relating to this response, or the application in general, she is respectfully requested to contact the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,

HUNTON & WILLIAMS LLP

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